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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/217,324	03/24/1994	WILLIAM R.A. OSBORNE	163363	9058

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EXAMINER

WOITACH, JOSEPH T

ART UNIT

PAPER NUMBER

1632

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39

Please find below and/or attached an Office communication concerning this application or proceeding.

File

# Office Action Summary

Application No.  
08/217,324

Applicant(s)  
Osborne et al.

Examiner  
Joseph Weitach

Art Unit  
1632



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Sep 30, 2002
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
- ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other:

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### **DETAILED ACTION**

This is an original application filed March 24, 1994.

Applicant's amendment filed September 30, 2002, paper number 38 has been received and entered. Claims 1, 5-10 have been amended. Claims 1-22 are pending and currently under examination.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Amendments to the claims to delete "autologous" have obviated the basis of the rejection.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Noishiki *et al.* (1992), Noishiki *et al.* ('261) and Zalewski *et al.* (1993).

Applicants summarize the basis of the rejection, and argue that it is not apparent how the teachings from two technologies can be combined to remedy the problems noted by Noishiki *et al.* Specifically, it is noted that the methods taught by Noishiki are operating procedures which prevent or diminish graft occlusion, noting that the procedure seeded autologous cells onto a Dacron graft and immediately returned the graft to the artery which was previously removed to generate the graft. It is noted that Noishiki *et al.* does not teach to culture cells or transduce the cell before seeding, and argue that the emphasis of the teaching is on thrombosis formation. In summarizing the teaching of Zalewski *et al.* Applicants note that reference provides no working examples more similar to a research plan and argue that lacking evidence supporting their proposal and assumptions there is little evidence that prolonged gene expression could be achieved. Further, it is noted that Applicants are unaware of such methods providing gene therapy to any patient to date. See Applicants' amendment, pages 3-6. Applicants' arguments have been fully considered but not found persuasive.

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First, it is noted, that the test for combining references is not what the individual references themselves suggest, but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). For the purpose of combining references, those references need not explicitly suggest combining teachings, much less specific references. *In re Nilssen*, 7 USPQ2d 1500 (Fed. Cir. 1988). The present invention is drawn to a product comprising a tubular elongated member onto which transduced smooth muscle cells are immobilized and allowed to express a gene of interest. At the time of filing artificial grafts were known and used to replace various parts of the vascular system. Further, as taught in Noishiki *et al.* arterial grafts comprising smooth muscle cells seeded onto the surface were used in attempts to reduce the thrombogenicity of the graft. Examiner would agree that the surgical methodology taught in Noishiki *et al.* would not lead one to methods of culturing cells or transducing cells, however these are not the teachings relied upon in Noishiki *et al.* Rather, Noishiki *et al.* is relied upon for demonstrating that vascular prostheses seeded with vascular smooth muscle cells were known and used at the time of filing. Further, the teaching of Noishiki *et al.* is relied upon for the state of the art and to demonstrate the problems associated with artificial arterial graft, specifically the problem of significant thrombogenicity. Noishiki *et al.* teach that administration of heparin may result in antithrombotic affects, however over 92% of the heparin is released is released over a short period of time and that longer term solutions should be pursued. At the time of filing Zalewski *et al.* teach a long term solution and methods of inhibiting intravascular blockage

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through antithrombotic treatment to ameliorate this art recognized problem. Specifically, Zalewski *et al.* teach that smooth muscle cells transduced with genes to express antithrombotic proteins could be used. Examiner agrees that Zalewski *et al.* does not provide any specific reduction to practice of the proposed invention for treatment, however Zalewski *et al.* does teach that the feasibility of transfecting smooth muscle cells and provides evidence that the various anti-thrombotic factors proposed would be effective. Note that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See *In re O'Farrell*, 7 USPQ2d 1673 (CAFC 1988). In the instant case Zalewski *et al.* provides a reasonable expectation of success by demonstrating the recombinantly generated anti-thrombotic proteins had functional activity. Additionally, it is noted that the instant specification does not provide (or require) a reduction to practice, and provides similar results and guidance to that taught in Zalewski *et al.* exemplifying that smooth muscle cell can be transduced to express a marker gene. It is well established in case law that a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. *In re Burkel*, 201 USPQ 67 (CCPA 1979). Furthermore, in the determination of obviousness, the state of the art as well as the level of skill of those in the art are important factors to be considered. The teaching of the cited references must be viewed in light of these factors. In the instant case, clearly vascular grafts seeded with smooth muscle cells were known at the time of filing and the limitation and problem for use of such grafts was the endothelialization of and blockage of the grafts once they were implanted. Further, at the time

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of filing clearly a more long term solution and treatment of intravascular blockage was under investigation. Zalewski *et al.* teach that a long term solution is the expression of recombinant anti-thrombotic proteins in smooth muscle cells and provides the preliminary evidence that such methodology can be practiced and would be effective. Given the knowledge and level of skill in the art, the artisan would have used the results present by Zalewski *et al.* to provide for transduced smooth muscle cells as a source of cells in the grafts taught by Noishiki *et al.* One of skill in the art would have been motivated to use the transduced cells for a more long term anti-thrombotic effect and to produce a graft more resistant to blockage. Zalewski *et al.* provides the evidence that cells can be transduced and the recombinant proteins produced have anti-thrombotic effects. Additionally, Noishiki *et al.* provide evidence that smooth muscle cells can be successfully immobilized onto an artificial graft. Therefore, in light of the evidence as a whole there would have been a reasonable expectation of success.

Thus, the claimed invention as a whole was *prima facie* obvious, and therefore, the rejection is maintained.

### ***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

  
DEBORAH J. REYNOLDS  
SUPERVISORY PATENT EXAMINER  
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